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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,581	07/31/2003	Anne-Marie Rodriguez	0857/70669	5002

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EXAMINER	
HAMA, JOANNE	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
09/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,581	RODRIGUEZ ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9-12,25-28,48 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,9-12,25-28,48 and 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 7, 2009 has been entered.

Claims 6, 8, 13-24, 29-47, 49, 50 are cancelled. Claim 25 is amended.

Claims 1-5, 7, 9-12, 25-28, 48, 51-54, drawn to an isolated multipotent human stem cell, are under consideration.

Maintained Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 9-12, 25-28, 48, 51-54 remain rejected in modified form under 35 U.S.C. 103(a) as being unpatentable over Katz et al., PCT Publication No. WO 00/53795, publication date, September 14, 2000, previously cited, Akanbi et al., 1994, J. Anim. Sci., 72: 2828-2835, previously cited, Hedrick et al.,

US Patent Application US 2003/0082152, published May 1, 2003, previously cited, Haynesworth et al., US Patent 5,733,542, patented March 31, 1998, previously cited Tremain et al., 2001, Stem Cells, 19: 408-418, Djian et al., 1983, J. Clin. Invest. 72: 1200-1208, Young et al., 1996, Blood, 87: 545-556, for reasons of record, June 25, 2008, January 26, 2009.

Applicant's amendment prompted the rejection to be modified. As such, the modification to the rejection is as follows. Response to Applicant's rebuttals of July 7, 2009 follows the modified rejection.

With regard to obtaining cells that adhered to the culture plate 12 hours after starting the culture (claim 25, steps c) and d)), the art teaches that stem cell lines originate from a single cell. To obtain these single cells, the art teaches that single cell-derived colonies can be isolated by using cloning cylinders and that the single cells can be tested for colony-forming efficiency, which is a predictor for life span and differentiation potential of the cell (Tremain et al., page 409, 2nd col. under Isolation and Culture of Human MSCs). In addition to using a cloning ring to isolate a single cell, the art teaches that a period of 12 hours is sufficiently long to allow adherence of cells, but is too brief for appreciable replication (Djian et al., page 1201, 2nd col., 1st parag. under Primary culture and cloning of adipocyte precursors). As such, allowing cells to adhere for 12 hours maximizes the number of cells that adhere to the plate and minimizes any confusion that two cells sitting next together are two different cells that plated next to each other or is the result of cell division. As such, an artisan would plate cells for 12 hours.

With regard to the limitation that the CA cells are cultured for 50-80 population doublings and diluting the cells 2-3 fold at each transfer (claim 25, step e)), the art teaches that primitive quiescent cells are retained in bulk expansion cultures and that the cell production capacity of the expanded cell product can largely be attributed to cells exhibiting quiescent behavior during culture. Cells labeled with PKH26 fluorescent dye can be identified to be proliferating or quiescent, as demonstrated by the amount of dye labeling the cell. Quiescent cells retained the most dye (and were see as dye^{bright} cells), as the fluorescence is reduced following cell division. Quiescent cells that retained more dye were shown to proliferate more and produced progeny that included multilineage colony forming cells. Thus, these cells were demonstrated to be stem cells (Young et al., abstract). Given these teachings, an artisan would have performed bulk culture, such as that taught by Young et al., in order to identify stem cells.

Applicant's arguments filed July 7, 2009 have been fully considered but they are not persuasive.

Applicant indicates that the recited method of claim 25 involves performing a number of steps which allows one to obtain a highly homogeneous population of stem cells with novel properties. The method conceived by the inventors as one which would allow the selection of a stem cell population comprising stem cells having the novel phenotype of the claimed cells and no other cell types. Steps a)-g) allow an artisan to obtain a novel stem cell population which is highly homogeneous and HLA class I negative. Step e) allows for selection of true

stem cells and an increase in their number because most of the other cell types present after step d) (e.g. precursor cells) die before 50 to 80 population doublings. (Applicant's emphasis, Applicant's response, pages 8-12). In response, this is not persuasive. As discussed above, the art provides guidance for an artisan to make single cell clones such that stem cells can be identified. Tremain et al. teach that it is routine for an artisan to select single cells and test them for colony-forming efficiency. An artisan would also have performed the bulk culture method taught by Young et al., in order to confirm that the cells identified as stem cells in Tremain et al.'s assay are in fact stem cells. Given that these method steps are routine at the time of filing, an artisan would have arrived at the claimed invention. With regard to Applicant indicating that the claimed cells have a particular characteristic (that they are HLA class I negative), an artisan would have arrived at the claimed cells with the recited characteristics, using the above cited references. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best,

Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Applicant indicates a surprising effect. Applicant indicates that the cells in the CA population in steps a)-d) are HLA Class I positive, but during the course of step e) becomes negative. The effect of the number of population doublings on the HLA Class I phenotype of the CA population was thus totally unexpected. Applicant indicates that there was no reason to expect this change would occur and the skilled artisan had no reason to carry out step e) (Applicant's emphasis, Applicant's response, page 12). In response, this is not persuasive. While Applicant identified a characteristic of the claimed cells, identification of a new characteristic on a known product does not render the instant invention novel. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004). With regard to carrying out step e), Young et al. teach that bulk culture identifies quiescent stem cells.

Applicant indicates that the homogeneity or the claimed cell population and the fact that it contains a high number of cells are two essential pre-

requisites to using stem cells in therapeutic and cosmetic applications. An HLA Class I negative phenotype is also an important pre-requisite to envisaging allo-transplantation of these cells in a human being with no risk of rejection (page 14, lines 11-12 of the specification, example 12.2.2) (Applicant's emphasis, Applicant's response, page 13). In response, the Examiner does not doubt the importance of the use of stem cells. However, the combined teachings of Katz et al., Akanbi et al., Hedrick et al., Haynesworth et al., Tremain et al., Djian et al., and Young et al., would have lead an artisan to the claimed cells with the recited characteristics.

Applicant provides a chart that displays the method steps of claim 25 and indicates the presence or absence of these steps in the cited documents as "yes" or "no." Applicant indicates that steps a), e), f), and g) are not disclosed and steps c) and d) are not clearly disclosed in the cited references. As indicated in section 3-1, above, performing all steps of this method (with the exception of step f)) is essential to obtain the claimed cells (Applicant's emphasis, Applicant's response, pages 13-18). In response, this is not persuasive. With regard to step a), obtaining adipose tissue from a new born to an 8 year old child, Applicant's table on page 13 of Applicant's response indicates that Akanbi et al. teach one-day old pig cells and not the claimed invention of cells from human adipose tissue obtained from a human from newborn to 8 years old. In response, the Examiner relied on the combined teachings of Katz et al. for teaching that stem cells can be obtained from human adipose tissue and Akanbi et al. for teaching that adipose precursor cells from young animals replicate faster and/or contain

more clones capable of full differentiation into adipocytes than cells from older animals (Akanbi et al., page 2828, 2nd col., 1st parag.). Given these teachings that there are advantages of using a cell from a juvenile animal from that over an adult, an artisan would have modified Katz et al.'s teaching and obtained adipose tissue from young humans and addresses the limitation of step a). With regard to the limitations of steps e) and f), the Examiner addressed this issue indicating the teachings of Young et al., above. With regard to g), it is well recognized in the art to obtain stem cells for therapeutic applications. For example, Young et al. teach obtaining hematopoietic stem cells for transfusion patients (Young et al., page 545, 1st col., 1st parag.). As such, an artisan would have identified stem cells (those that stained dye^{bright}) and collected them.

Applicant indicates that Akanbi et al. teach away from using adipose tissue from a younger subject. Akanbi et al. teach that adipose precursor cells obtained from adipose tissue of younger pigs divide faster than those obtained from older pigs. However, adipose precursor cells are not the cell type which the skilled person is seeking to isolate according to the subject invention. Precursor cells are indeed different from stem cells. In particular, their potential for differentiation is much more limited than stem cells. Further, the objective of the disclosed method and claimed in the subject matter is to isolate a highly homogenous stem cell population. A precursor cell is not the cell type envisioned to be isolated and also is indicative of a contaminant. The skilled artisan seeking to obtain a highly homogenous stem cell population would be driven to select a tissue in which precursor cells are present in a lower number

and/or in which they proliferate at a slower rate (Applicant's emphasis, Applicant's response, page 18). In response, this is not persuasive. The Examiner was not relying on Akanbi et al. for teaching adipose precursor cells. Rather, the Examiner relied on Akanbi et al. for teaching that there are different characteristics in adipose precursor cells obtained from newborn animals versus that of adult animals and that cells from newborns have better potential for producing a larger quantity of differentiated cells. Akanbi et al.'s teaching does not teach away from the claimed invention because ultimately, an artisan would want stem cells whose descendants produce large amounts of differentiated cells. Those cells would be cells from a juvenile. An artisan does not necessarily rely on Akanbi et al. for implying that mulitpotent stem cells from young animals divide faster than multipotent stem cells from adult animals because Young et al. teach that the multipotent stem cell divides rarely. With regard to Applicant indicating that the precursor cell is not the cell an artisan is seeking to isolate, and that the precursor cell is a contaminant, the above combined teachings do not lead an artisan to isolation of an adipose precursor cell or a mixture of cells. Rather, the combined teachings provide guidance for an artisan to take adipose tissue from a juvenile because Katz et al. teach that adipose tissue is a source of stem cells. The tissue is obtained from a juvenile because Akanbi et al. teach that cells from juveniles have better potential to produce more differentiated cells. With regard to selecting cells that have been plated for 12 hours and subjecting them to culture conditions that expand them until a quiescent population is

obtained, Tremain et al., Dijan et al., and Young et al. teach that these are routine steps used to identify and isolate single clones of stem cells.

Thus, the claims remain rejected.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632